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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	MAY 01	New CAS web site launched
NEWS	3	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS	4	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS	5	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS	6	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS	7	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS	8	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS	9	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS	10	JUN 29	STN Viewer now available
NEWS	11	JUN 29	STN Express, Version 8.2, now available
NEWS	12	JUL 02	LEMBASE coverage updated
NEWS	13	JUL 02	LMEDLINE coverage updated
NEWS	14	JUL 02	SCISEARCH enhanced with complete author names
NEWS	15	JUL 02	CHEMCATS accession numbers revised
NEWS	16	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS	17	JUL 16	CAplus enhanced with French and German abstracts
NEWS	18	JUL 18	CA/CAplus patent coverage enhanced
NEWS	19	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS	20	JUL 30	USGENE now available on STN
NEWS	21	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	22	AUG 06	BEILSTEIN updated with new compounds
NEWS	23	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	24	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS	25	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 11:29:14 ON 20 AUG 2007

=> file medline, biosis, wpids
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:29:31 ON 20 AUG 2007

FILE 'BIOSIS' ENTERED AT 11:29:31 ON 20 AUG 2007
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=> (toll-like receptor 8)
(TOLL-LIKE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s (TLR-8)
L1          76 (TLR-8)

=> s l1 and (Toll-like receptor-8)
L2          50 L1 AND (TOLL-LIKE RECEPTOR-8)

=> s l2 and (2-aminopyridine)
L3           0 L2 AND (2-AMINOPYRIDINE)

=> s l2 and (imidazoquinoline)
L4           5 L2 AND (IMIDAZOQUINOLINE)

=> d l4 ti abs ibib tot

L4   ANSWER 1 OF 5  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
TI   The antitumoral mode of action of imiquimod and other imidazoquinolines.
AB   Imiquimod, the lead compound of the imidazoquinoline family of
     nucleoside analogues, has shown good efficacy against a variety of tumors
     of different origin.  The mode of action of imiquimod and related
     compounds, which we have begun to understand in sorne detail in recent
     years, is complex and interesting inasmuch as it appears to comprise
     several presumably mutually enhancing components.Predominant amongst its
     actions is the induction of pro-inflammatory cytokines through agonistic
     activity towards Toll-like receptor (TLR)-7 and TLR-8,
     and consecutively, activation of the central transcription factor NF-kappa
     B.  This activity stimulates the production of pro-inflammatory cytokines,
     chemokines and other mediators resulting in activation of
     antigen-presenting cells and the mounting of a profound Th1-weighted
     antitumoral cellular immune response.  In addition, there are a number of
     secondary effects on the molecular and cellular level that can be
     explained through the activation of NF-kappa B.  The pro-inflammatory
     activity of imiquimod appears to be augmented by suppression of a negative
     regulatory feedback mechanism which normally limits inflammatory
     responses.  This is achieved independent of TLR-7 and TLR-
     8 through interference with adenosine receptor signaling pathways,
     particularly the A(2A) subtype, and receptor-independent reduction of
     adenylyl cyclase activity.  Finally, at higher, albeit therapeutically
     relevant concentrations, imiquimod exerts a pro-apoptotic activity against
     tumor cells.  Induction of apoptosis by imiquimod appears to be dependent
     on Bcl-2 proteins and involves caspase activation.The combination of
     multiple, presumably synergistic anti-tumoral functions by a single
     compound represents an interesting principle of pathogenesis-oriented,
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anti-neoplastic therapy.
ACCESSION NUMBER: 2007:215335 BIOSIS
DOCUMENT NUMBER: PREV200700214472
TITLE: The antitumoral mode of action of imiquimod and other imidazoquinolines.
AUTHOR(S): Schoen, Margarete; Schoen, Michael P. [Reprint Author]
CORPORATE SOURCE: Univ Wurzburg, Rudolf Virchow Ctr, DFG Res Ctr Expt Biomed, Versbacher Str 9, D-97078 Wurzburg, Germany michael.schoen@virchow.uni-wuerzburg.de
SOURCE: Current Medicinal Chemistry, (2007) Vol. 14, No. 6, pp. 681-687.
ISSN: 0929-8673.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2007
Last Updated on STN: 28 Mar 2007

L4 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI The small antitumoral immune response modifier imiquimod interacts with adenosine receptor signaling in a TLR7-and TLR8-independent fashion.
AB Imiquimod, a small-molecule immune response modifier of the imidazoquinoline family, has shown profound antitumoral and antiviral efficacy both in vitro and in clinical applications in vivo. It has been demonstrated that this activity is mediated through the Toll-like receptor (TLR)7- and TLR8-signaling cascade resulting in the secretion of proinflammatory cytokines and, consecutively, induction of a tumor-directed cellular immune response. In addition, imiquimod exerts a direct proapoptotic activity in tumor cells. We demonstrate here that imiquimod induces activation of the transcription factor NF-kappa B and the downstream production of proinflammatory cytokines in the absence of TLR7 and TLR8. In Chinese hamster ovary cells stably transfected with the human adenosine receptor subtypes, we then show in radioligand-binding competition experiments that imiquimod binds to adenosine receptors at concentrations relevant in clinical settings, with highest affinities to the A(1) and A(2A) subtypes. The effect on the receptor-mediated activation of adenylyl cyclase was also studied, and these experiments revealed that imiquimod acts as an adenosine receptor antagonist. In addition, imiquimod had an inhibitory effect on adenylyl cyclase activity downstream from the receptor. Finally, using transformed human keratinocytes, we provide experimental evidence that imiquimod and A2A adenosine receptor-specific compounds similarly induce proinflammatory cytokines in the absence of immune cells. Thus, imiquimod appears to suppress an important feedback mechanism of inflammation by antagonism of adenosine receptor-dependent increase of cAMP and a concomitant receptor-independent inhibition of cAMP production. These novel mechanisms presumably act synergistic with the positive induction of proinflammatory cytokines and can, at least in part, explain the profound inflammation observed in some patients in vivo.
ACCESSION NUMBER: 2006:603217 BIOSIS
DOCUMENT NUMBER: PREV200600613866
TITLE: The small antitumoral immune response modifier imiquimod interacts with adenosine receptor signaling in a TLR7-and TLR8-independent fashion.
AUTHOR(S): Schoen, Michael P. [Reprint Author]; Schoen, Margarete; Klotz, Karl-Norbert
CORPORATE SOURCE: Univ Wurzburg, Rudolf Virchow Ctr, DFG Res Ctr Expt Biomed, Versbacher Str 9, D-97078 Wurzburg, Germany michael.schoen@virchow.uni-wuerzburg.de
SOURCE: Journal of Investigative Dermatology, (JUN 2006) Vol. 126, No. 6, pp. 1338-1347.
CODEN: JIDEAE. ISSN: 0022-202X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Nov 2006

L4 ANSWER 3 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Polymorphisms in TLR7 and 8 affect severity of hepatic fibrosis and inflammation in individuals infected with the hepatitis C virus from a single source.
AB Background and Aims: Toll-like receptors (TLRs) are type I transmembrane proteins, which are highly conserved through evolution. They activate innate immunity by recognizing and binding. to a wide variety of pathogenic substances. TLR7 and 8 both respond to the synthetic imidazoquinoline compounds, known to have anti-viral properties. TLR7 and probably TLR8 have also been demonstrated to recognize single stranded viral RNA. This study aimed to assess the involvement of inherited variations in TLR7 and 8 in determining disease outcome in HCV infected individuals. Methods: 223 women all exposed to HCV genotype 1b from a single donor, and including 85 who had spontaneously cleared the virus and 138 chronically infected, were genotyped for TLR 7 and 8 polymorphisms and haplotype tagging was performed. The frequencies of these polymorphisms were then compared with disease activity and severity. Results: TLR 7 and 8 genotypes were compared with HCV PCR status, ALT levels and liver histology. There was no association between HCV PCR status and the TLR polymorphisms. Of the 5 SNPs examined in TLR8, wild types were associated with significantly worse fibrosis for 2 SNP loci (TLR8C (C401T); 1.38 vs 0.78, $p = 0.03$, TLR8D (C426T); 1.39 vs. 0.70, $p = 0.018$). Degree of inflammation was worse in TLR8B (A796C) wild type; 5.1 vs. 4.2, $p = 0.008$, and this group also had higher ALT levels; 66 vs. 41, $p = 0.018$. TLR7B (C149T) was associated with lower inflammation and 4.4 vs. 5.7, $p = 0.015$ ALT levels; 47.8 vs. 73.4, $p = 0.014$. On analysis of haplotypes, those containing the minor allele for TLR8A or TLR8B had significantly less fibrosis ($p = 0.025$, $p < 0.01$, respectively). Haplotypes containing the minor allele for TLT7B had significantly lower inflammatory scores, $p < 0.025$. No haplotype was associated with viral clearance. Conclusion: Consistent with prior functional data regarding viral clearance, HCV viral clearance was not associated with any of the TLR 7 or 8 SNPs examined in this study. However, SNPs in TLR 7 and 8 were associated with a lesser degree of hepatic inflammation and fibrosis. Further functional characterisation of these SNPs could provide important information on the response of the host to HCV infection.
ACCESSION NUMBER: 2006:499496 BIOSIS
DOCUMENT NUMBER: PREV200600505816
TITLE: Polymorphisms in TLR7 and 8 affect severity of hepatic fibrosis and inflammation in individuals infected with the hepatitis C virus from a single source.
AUTHOR(S): Goulding, Carol A.; Mc Manus, Ross; Murphy, Anne; Mac Donald, George S.; Dring, Megan; Hegarty, John; Kiernan, Susan Me; Kelleher, Dermot
SOURCE: Gastroenterology, (APR 2006) Vol. 130, No. 4, Suppl. 2, pp. A780.
Meeting Info.: Digestive Disease Week Meeting/107th Annual Meeting of the American-Gastroenterological-Association. Los Angeles, CA, USA. May 19 -24, 2006. Amer Gastroenterol Assoc Inst.
CODEN: GASTAB. ISSN: 0016-5085.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Oct 2006
Last Updated on STN: 4 Oct 2006

L4 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Immune modulation and apoptosis induction: Two sides of the antitumoral activity of imiquimod.
AB Imiquimod, the first member of the imidazoquinoline family of immune response modifiers, has proven good clinical efficacy against basal

cell carcinomas and actinic keratoses in several independent studies. In addition, there is recent evidence that imiquimod is also efficacious against other tumors such as cutaneous metastases of malignant melanoma or vascular tumors. Imiquimod exerts its antitumoral effect, at least in part, through binding to TLR-7 and TLR-8 on dendritic cells followed by secretion of a multitude of proinflammatory cytokines. The net result of this proinflammatory activity is a profound tumor-directed cellular immune response. However, recent experimental and clinical data indicate that imiquimod also possesses considerable direct proapoptotic activity against tumor cells both in vitro and in vivo. This novel mode of action appears to be independent of membrane bound death receptors, but involves caspase activation. Induction of apoptosis by imiquimod is, at least in part, presumably mediated through Bcl-2-dependent release of mitochondrial cytochrome c and subsequent activation of caspase-9. The structural analogue, resiquimod, exhibited very limited, if any, such proapoptotic activity, possibly due to its lacking ability to enter the cell. Bypassing molecular mechanisms of apoptosis deficiency by a topical compound may be of great utility for treating certain cutaneous tumors.

ACCESSION NUMBER: 2004:282528 BIOSIS
DOCUMENT NUMBER: PREV200400282627
TITLE: Immune modulation and apoptosis induction: Two sides of the antitumoral activity of imiquimod.
AUTHOR(S): Schoen, M. P. [Reprint Author]; Schoen, M.
CORPORATE SOURCE: Rudolf Virchow CtrDFG Res Ctr Expt Biomed, Univ Wurzburg, Versbacher Str 9, D-97078, Wurzburg, Germany michael.schoen@virchow.uniwuerzburg.de
SOURCE: Apoptosis, (May 2004) Vol. 9, No. 3, pp. 291-298. print. ISSN: 1360-8185 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Jun 2004
Last Updated on STN: 9 Jun 2004

L4 ANSWER 5 OF 5 WPIDS COPYRIGHT 2007 THE THOMSON CORP on STN

TI Immunostimulatory combination for inducing toll like receptor 8-mediated biological activity e.g. synthesis of cytokine for treating e.g. cancer comprises toll like receptor 8 agonist in combination with immunostimulatory oligonucleotide
AN 2006-424284 [43] WPIDS
AB WO 2006063152 A2 UPAB: 20060706
NOVELTY - An immunostimulatory combination (C1) comprises a toll like receptor (TLR)8 agonist in combination with an immunostimulatory oligonucleotide to induce at least one TLR8-mediated biological activity.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for inducing TLR8-mediated biological activity in immune cells, involving contacting the immune cells with (C1) to increase a TLR8-mediated biological activity of the cells to a greater extent than contacting the immune cells with the TLR8 agonist without the immunostimulatory oligonucleotide.

ACTIVITY - Immunostimulant; Cytostatic; Antiinflammatory; Dermatological; Immunosuppressive; Virucide; Antibacterial; Fungicide; Antimalarial; Respiratory-Gen.; Keratolytic; Anti-HIV; Antiasthmatic; Antiallergic; Neuroprotective; Vulnerary.

MECHANISM OF ACTION - Toll like receptor (TLR)8 agonist; Tumor necrosis factor (TNF) production inhibitor; Interleukin (IL)-12 production inhibitor. A combination (test) comprising 2-propylthiazolo(4,5-c)quinolin-4-amine (IRM) (3 muM) and 5'-TCGTCGAACGTTCGAGATGAT-3' (CpG ODN M352) (10 muM) was prepared and tested for TLR8 agonistic activity using HEK 293 cells. Cell aliquots were

treated by (C1). As controls, some cell aliquots were incubated with 3 muM of IRM only (positive control) and other cell aliquots were incubated with (CpG ODN M352) only (negative control). In all cases, the cells were incubated overnight at 37degreesC with 5% CO2 and 98% humidity. Each well of the plate was read on a L-max luminometer. The data was expressed as fold increase of luciferase induction in cell aliquots incubated with the indicated stimulant compared to the negative control. The fold increase for test/positive control/negative control was found to be approximately 104/approximately 39/approximately 0.5.

USE - For inducing at least one toll like receptor (TLR) 8-mediated biological activity (e.g. synthesis of a cytokine such as tumor necrosis factor (TNF) and interleukin (IL)-12, synthesis of a chemokine, synthesis of co-stimulatory markers, maturation of antigen-presenting cells and proliferation of B lymphocytes) in immune cells (e.g. peripheral blood mononuclear cells (PBMCs) and monocyte-derived dendritic cells) (claimed). The combination is used for treatment of cancer; lupus erythematosus; viral diseases; bacterial diseases; other infectious diseases such chlamydia; fungal diseases including aspergillosis, histoplasmosis, cryptococcal meningitis and parasitic diseases (including malaria, pneumocystis carnii pneumonia, leishmaniasis, cryptosporidiosis, toxoplasmosis and trypanosome infection); neoplastic diseases such as intraepithelial neoplasias, cervical dysplasia, actinic keratosis, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, melanoma, renal cell carcinoma, leukemia; TH2-mediated atopic diseases such as atopic dermatitis and eczema, eosinophilia, asthma, allergy, allergic rhinitis and Ommen's syndrome; autoimmune diseases such as systemic lupus erythematosus, thrombocythemia, multiple sclerosis, discoid lupus, alopecia areata; and diseases associated with wound repair such as inhibition of keloid formation and other types of scarring (e.g. enhancing wound healing, including chronic wounds). The combination can be used in the treatment of humans, rodents, dogs, cats, horses, pigs, sheep, goats, or cows.

ADVANTAGE - The combination can provide greater immunostimulatory activity than either component can provide alone i.e. can provide at least two-fold (preferably at least three-fold, especially at least five-fold) even greater increase in at least one toll like receptor (TLR) 8-mediated biological activity compared to that induced by a TLR8 agonist administered without the immunostimulatory oligonucleotide; can provide synergistic immunostimulatory activity; improves the efficacy of certain immunological treatments that involves a TLR8-mediated biological activity; enhances vaccine-induced TLR8-mediated biological activity to improve the efficacy of the vaccine - even to the point of enabling a vaccine previously considered ineffective to be considered effective; and can enable some immunological treatments to be clinically and/or commercially viable that previously had been considered clinically and/or commercially undesirable because of cost of a component of the treatment, availability of all components and/or the amount of a component (e.g. an antigen) previously considered necessary to generate an effective immune response also generated an undesirable level of side effects.

ACCESSION NUMBER: 2006-424284 [43] WPIDS
DOC. NO. CPI: C2006-133823 [43]
TITLE: Immunostimulatory combination for inducing toll like receptor 8-mediated biological activity e.g. synthesis of cytokine for treating e.g. cancer comprises toll like receptor 8 agonist in combination with immunostimulatory oligonucleotide
DERWENT CLASS: B02; B03; C02
INVENTOR: GORDEN K B; QIU X; WIGHTMAN P D
PATENT ASSIGNEE: (MINN-C) 3M INNOVATIVE PROPERTIES CO
COUNTRY COUNT: 111

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006063152	A2	20060615	(200643)*	EN	39[9]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006063152	A2	WO 2005-US44448	20051208

PRIORITY APPLN. INFO: US 2004-634146P 20041208